

**REMARKS**

In claim 3, the word "whether" has been replaced with "how" for consistency with independent claims 9, 11 and 13.

The word "test" has been deleted from "test compound" in independent claims 3, 9, 11 and 13 for internal consistency.

In claim 9, "coordinates" has been replaced with "intersidechain distances" for consistency with claim 3.

**Claim Rejections – 35 U.S.C. § 112, Second Paragraph**

The Examiner objected to claims 3, 6, 9, 11, 13, 15 and 20-24 under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

The Examiner objected that claims 3, 9, 11 and 13 recite at step (a) "wherein the program displays the quaternary structure of the ligand binding site", making it allegedly unclear whether this is an active method step or a limitation (characteristic) of the program. Claims 3 and 9 have been reworded to recite an active method step, "the program displaying all or part of the fitted quaternary structure of the insulin receptor including the ligand binding site." Claims 11 and 13 have been modified to refer to "the program displaying all or part of the fitted quaternary structure of the insulin receptor including the residues". The reference to the fitted quaternary structure of the "insulin receptor" has been inserted in all independent claims for clarity. Applicants have also removed step labels "a)" and "b)" since any required order of steps is implicit in the currently amended claim wording.

The Examiner objected that claims 3, 9, 11 and 13 recite a step of "next determining whether a test compound modulates insulin receptor activity" because it is allegedly unclear what the relationship of this step is to step (a) and step (b) which are computerized steps of comparing structural coordinates. Claims 3 and 9 recite "comparing the structural coordinates of the compound to the structural coordinates of the ligand binding site and determining whether the compound fits spatially into the ligand binding site." The subsequent paragraph has been amended to recite "wherein if the compound fits spatially into the ligand binding site," in front of the phrase "next determining whether the compound modulates insulin receptor activity." This amendment clarifies the relationship of this step to the preceding steps.

Currently amended claims 11 and 13 refer to "comparing the structural coordinates of the compound to the structural coordinates of the residues and determining whether the compound interacts with the residues". The subsequent paragraph has been amended to recite "wherein if the compound fits spatially between the residues," in front of "next determining whether the compound modulates insulin receptor activity." This amendment clarifies the relationship of this step to the preceding steps.

#### **Claim Rejections – 35 U.S.C. § 112, First Paragraph**

The Examiner rejected claims 11 and 13 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The Examiner stated that claims 11 and 13 recite "at least one residue between amino acids 250 to 280 of SEQ ID NO:16", however, there is no indication about the nature of SEQ ID NO:16, for example, whether or not it is the ligand binding domain of a particular monomer of insulin receptor.

SEQ ID NO:16 of the DNA and amino acid sequence listing submitted for this application corresponds to the alpha subunit of insulin receptor, and this sequence is shown in Figure 12 in the application as filed. The claims have been revised to refer to the amino acids 250-280 shown in "Figure 12" rather than refer to "SEQ ID NO:16". Claims 23 and 24, which depend from claims 11 and 13, respectively, have also been amended to refer to "Figure 12" instead of SEQ ID NO:16. As noted in the Applicants' prior response, support for the 250-280 range is found in the specification on page 51, lines 23-25 which recites cam-like structures formed by a loop of amino acids from 250-280. Table 2 also refers to the cam-loop segment of the cys-rich region and its functional significance is further detailed in Example 7 on pages 53 to 55. Example 7 refers to Figures 5 and 9 that model the mechanism of insulin receptor activation, and also to Fig. 7, which in Fig. 7c shows the cam-loop segment corresponding to amino acid nos. 250 to 280.

Explanation for the significance of the cam-like structures in identifying modulators of insulin receptor activity is found, for example, on page 25, line 25 to page 26, line 20 which describes that the two cams change the conformation of the insulin receptor. It is further described that a potential modulator may interact with at least one insulin receptor residue listed in Table 2 on the cam-loop segment of the Cys-rich region. Additional description is also found, for example, on page 32, line 26 to page 33, line 2.

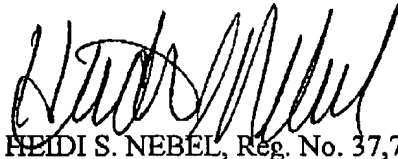
#### **Claim Rejections – 35 U.S.C. § 102**

The Examiner objected to claim 25 under 36 U.S.C. § 102 as being anticipated by WO 99/28347. Claim 25 has been deleted.

**Conclusion**

Please charge deposit account number 26-0084 for \$60.00, the fee for a one-month extension of time, which is respectfully petitioned. It is not believed any additional fees or extensions of time are due in connection with this amendment; however, consider this a request for any extension inadvertently omitted, and charge any additional fees to Deposit Account No. 26-0084. The Examiner is invited to contact the undersigned at the number below if it is felt that this would aid prosecution.

Respectfully submitted,



HEIDI S. NEBEL, Reg. No. 37,719  
MCKEE, VOORHEES & SEASE, P.L.C.  
801 Grand Avenue, Suite 3200  
Des Moines, Iowa 50309-2721  
Phone No: (515) 288-3667  
Fax No: (515) 288-1338  
CUSTOMER NO: 22885  
Attorneys of Record

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